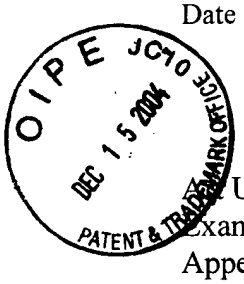
Express Mail Label No.: EV475167645US
Date of Deposit: December 15, 2004

Attorney Docket No. 23239-301C



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

Art Unit: 1635
Examiner: Janet L. Epps-Ford
Appellants: Ellington et al.
Serial No.: 09/883,119
Filed: June 14, 2001
For: Regulatable, Catalytically Active Nucleic Acids

Boston, MA 02111
December 15, 2004

Mail Stop Appeal Brief--Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

Sir:

In regard to the referenced application, Appellants submit this Appeal Brief, pursuant to 37 C.F.R. § 41.37, in support of their Notice of Appeal, dated October 15, 2004. With no extension of time, this Appeal Brief is due on or before December 15, 2004. A check for $250.00 (Check #19770) is enclosed to cover the fee for filing a brief in support of an appeal required under 37 C.F.R. § 1.17(c).

The Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to Deposit Account No. 50-0311, Reference 23239-301C.

This Brief has the following appendix:

Claims Appendix: Claims pending as of Advisory Action, mailed November 3, 2004.

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I. REAL PARTY IN INTEREST

The real party in interest is Archemix Corporation, the exclusive licensee of Board of Regents, The University of Texas System, the assignee of the application from all inventors.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no other related appeals or interferences which will directly affect, be directly affected by, or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Pending claims 1-6, 9-14, 128 and 137, as set forth in the Claims Appendix, are the subject of this appeal.

Claims 1-136 were included in the application as originally filed. Claims 1-14 and 128 were elected and claims 15-127 and claims 129-136 were withdrawn from consideration in response to a June 3, 2003 Restriction Requirement. Claims 1-6, 12-14, and 128 were amended, and claim 137 was added in response to a September 23, 2003 Office Action.

In the July 20, 2004 Final Office Action (the "Final Office Action"), claims 1-14,128 and 137 were rejected by the Examiner. Appellants' October 15, 2004 Response amended claims 1 and 128, and cancelled claims 7 and 8. In an Advisory Action mailed on November 3, 2004 (the "Advisory Action"), the Examiner indicated that these claim amendments would be entered, but maintained the rejections.

IV. STATUS OF AMENDMENTS

In response to the Final Office Action of July 20, 2004 Appellants filed an Amendment and Remarks on October 15, 2004 in which Appellants amended claims 1 and 128, and cancelled

claims 7 and 8. Appellants submitted these amendments in order to place the pending claims in better form for consideration on appeal, pursuant to 37 C.F.R. § 1.116(b). The Notice of Appeal was filed on October 15, 2004. Appellants received an Advisory Action dated November 3, 2004, which indicated that the amendments had been entered. The claims set forth in the Claims Appendix (section IX) reflect the fact that the amendments submitted on October 15, 2004 have been entered.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The subject invention involves regulatable, catalytically active nucleic acids ("RCANAs"). RCANAs may be used for regulating gene expression and in assays to detect the presence of ligands. The invention describes RCANAs that are identified through a selection process which involves the novel strategy of including the catalytic core in the selection process by using a randomized region which spans critical residues within the catalytic core itself to select for ligand dependent catalytically active nucleic acids. The broadest claim is claim 1. Claim 1 is directed towards a DNA polynucleotide comprising a catalytic domain and a regulatory domain, wherein the catalytic activity of the polyncucleotide is regulated by the interaction of a peptide effector with the regulatory domain of the polynucleotide. Materials and methods for identifying, isolating and creating peptide dependent RCANAs, are described throughout the specification, *e.g.*, at page 2 lines 20-23; page 3 lines 4-10; page 4 lines 6-10; page 13 lines 7-25; page 14 line 16 to page 15 line 2; page 15 lines 20-26; page 47 lines 21-25; page 31 lines 2-11; and in Example 3 (page 45) and Example 4 (page 57).

Additionally, several figures in the specification describe the methods for identifying and creating peptide dependent RCANAs as well sequences and structures of compositions of the

subject invention, and functional data for compositions of the subject invention. Figures 15(a), 15(b), 17(a) and 17(b) show an example of the sequence and structure of a starting pool for a ribozyme ligase used to select for peptide dependent RCANAs, which shows the randomized region overlapping with the catalytic domain. Figures 15(c) and 17(c) are schematic diagrams of a selection protocol that can be used to identify and isolate peptide dependent RCANAs, and Figure 22 is a flow chart describing a positive and negative selection method used to identify and isolate peptide dependent RCANAs. Figures 19(a) and 19(b) show the sequences and structures of several peptide dependent RCANAs (cyt18 dependent ribozyme ligases, described in Example 3, page 45). Figure 20 shows the binding specificity of a peptide dependent RCANA, and Figure 21 shows the binding and ligation activity of a peptide dependent RCANA (cyt18 dependent ribozyme ligase) as a function of protein concentration.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 1-6, 9-14, 128 and 137 stand rejected under 35 U.S.C. §112, first paragraph, for lack of written description.

Claims 1-2, 5, 9-10, 12-13, and 137 stand rejected under 35 U.S.C. §102(b) as being anticipated by George *et al.*, US Patent No. 5, 834,186.

VII. ARGUMENTS

A. The Rejection of Claims 1-6, 9-14, 128 and 137 under 35 U.S.C. §112, First Paragraph

1. Statement of the Relevant Law Pertaining to 35 U.S.C. § 112, First Paragraph Written Description Requirement

The established rule in relation to the §112, written description requirement is that the claimed invention is adequately described if the specification reasonably conveys to persons skilled in the art that the inventors invented or were in possession of the claimed subject matter

as of the filing date of the application (*In re Wertheim*, 541 F.2d 257,262, 191 USPQ 90, 97 (CCPA), *appeal after remand*, 646 F.2d 527, 209 USPQ 554 (CCPA 1981); *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000), *cert. denied*, 121 S. Ct. 1167 (2001)). The claimed subject matter need not be described *in haec verba* in the specification in order for the written description requirement to be fulfilled (*Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000)).

The burden is upon the Patent Office to establish a *prima facie* case that the written description requirement has not been met. The Examiner has the initial burden of presenting reasons or evidence supporting his/her position that the skilled artisan would not recognize the claimed invention in the specification (*Ex parte Sorenson*, 3 USPQ2d 1462, 1463 (BPAI 1987) (citing *In re Wertheim*, 541 F.2d 257, 192 USPQ 90 (CCPA 1976)).

If a *prima facie* case of lack of written description is established, the Appellants can rebut such case by evidence that shows that the application does in fact include an adequate written description of the invention (*In re Marzocchi*, 439 F.2d 220, 223-4, 169 USPQ 367, 369 (CCPA 1971)).

2. The Rejection of Claims 1-6, 9-14, 128 and 137 under 35 U.S.C. § 112, first paragraph is improper

Appellants respectfully submit that the rejection of claims 1-6, 9-14, 128 and 137 under 35 U.S.C. § 112, first paragraph, lack of written description, is improper because the Examiner has not established a *prima facie* case of lack of written description. In the alternative, Appellants argue that assuming *arguendo* that *prima facie* lack of written description has been established, it is rebutted by experimental evidence that the specification adequately describes the claimed invention.

The Examiner's position appears to be based on the following points:

(i.) The specification provides only one example of independent claim 1 (a polynucleotide that is regulated by a peptide effector) and thus provides insufficient written description to support the genus of polynucleotides and peptide effectors, encompassed by the instantly claimed invention (Final Office Action, page 3).

(ii.) Appellants have not demonstrated, apart from further experimentation, how to use the specific example set forth in the specification as filed to predict the structures of other regulated polynucleotides and their corresponding peptide effectors (Final Office Action, page 3).

(iii.) Examiner cites MPEP § 2163, which states "A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." (Final Office Action, page 3).

Appellants contend that the Examiner has not established a *prima facie* case of lack of written description under §112, first paragraph, because there is literal support in the specification for independent claim 1. As stated above in Section VII.A, it is not necessary that the specification provide literal support (*in haec verba*) for a claim in order for the claim to meet the written description requirement (*Purdue Pharma L.P.*, 56 USPQ2d at 1483). However, the Appellants submit that each of the elements of claim 1 has literal support throughout the specification.

"**A DNA polynucleotide that is regulated by a peptide effector**" of claim 1 finds literal support in the following passages:

Page 2, lines 20-23 of the specification states:

> It should be noted that the methods described herein may include any type of nucleic acid. For example, these methods are not limited to RNA based RCANAs, but also encompass DNA RCANAs and RNA or DNA RCANAs.

Page 3 lines 4-10 of the specification provides:

> The effector may be a peptide, a polypeptide, a polypeptide complex, or a modified polypeptide or peptide.....The effector may be activated by a second effector that acts on the first effector, which may be an inorganic or an organic molecule. The polypeptide, peptide or polypeptide complex can be either endogenous, *i.e.*, derived from the same cell type as the polynucleotide, or exogenous, *i.e.*, derived from a cell type different than the cell from which the polynucleotide is derived.

A "**regulatable, catalytically active polynucleotide having a catalytic domain and a regulatory domain, wherein the catalytic activity of the catalytic domain is regulated by the interaction of the peptide effector with the regulatory domain**" of claim 1 finds literal support in the following passages:

Page 4, lines 6-10 of the specification provides:

> The present invention includes RCANAs with catalytic activity that is regulated by a protein or peptide. One embodiment of the present invention involves the in vitro selection of RCANAs that are regulated by proteins. A selection scheme for RCANAs dependent on protein cofactors has been developed.

In page 13 lines 7-25 of the specification it is stated:

> To date, the present inventors have selected a number of protein and peptide dependent ribozyme ligases. One example is the isolation of a protein dependent, regulatable, catalytically active nucleic acid with an activity that was increased in a standard assay by 75,000-fold in the presence of its cognate protein effector, tyrosyl tRNA synthetase from *Neurospora* mitochondria (Cyt18). The Cyt18-dependent ribozyme was not activated by non-cognate proteins, including other tRNA synthetases.
>
> A protein-dependent, regulatable, catalytically active nucleic acid was also created and selected with an activity that was increased by 3,500-fold in the presence of its cognate protein effector, hen egg white lysozyme. The lysozyme-dependent ribozyme was not activated by most

non-cognate proteins, including T4 lysozyme, but was activated by a very closely related protein, turkey egg white lysozyme. Moreover, the protein-dependent ribozyme was inhibited by a RNA binding species that specifically bound to lysozyme. In other words, the activation of these protein-dependent ribozymes was highly specific.

A peptide dependent, regulatable, catalytically active nucleic acid was also created and isolated with activity which was increased by 18,000-fold in the presence of its cognate peptide effector, the arginine-rich motif (ARM) from the HIV-1 Rev protein. The Rev-dependent nucleic acid was not activated by other ARMs from other viral proteins, such as HTLV-I Rex. Using the present invention, regulatable, catalytically active nucleic acids may be developed that are regulated by any of a vast number of proteins.

Additionally, page 31, lines 2-11 of the specification provides the following definition:

As used herein, the term "regulatable, catalytically active nucleic acid" or "RCANA" means a ribozyme or nucleic acid enzyme that is regulated by an effector. The kinetic parameters of the RCANA may be varied in response to the amount of an effector, which may be an allosteric effector molecule. Just as allosteric protein enzymes undergo a change in their kinetic parameters or of their enzymatic activity in response to interactions with an effector molecule, the catalytic abilities of RCANAs may be similarly modulated by effectors. As demonstrated herein, the effectors may be small molecules, proteins, peptides, or molecules that interact with proteins, peptides, or other molecules. RCANAs transduce molecular recognition into catalysis upon interaction with an effector that interacts with a portion of the RCANA.

In addition to the passages cited above, experimental evidence provided in Examples 3 and 4, and the Figures corresponding to these examples (*e.g.*, Figures 15, 17, 19, 20, 21, 22, and 23) support that the Appellants were in possession of the subject invention at the time of filing. The Examiner herself notes that the specification provides experimental evidence of the claimed invention, through the Rev dependent RNA ligase ribozyme, found in Example 4. Despite all of this, the Examiner has found this written description unacceptable and argues that one example of independent claim 1 (a polynucleotide that is regulated by a peptide effector) is insufficient to support the genus of polynucleotides and peptide effectors, encompassed by the instantly claimed invention (Final Office Action, page 3).

Contrary to the Examiner's position, the specification as filed describes more than one species within the genus of polynucleotides regulated by a peptide effector. As stated above, the Appellants have provided several examples of polynucleotides that are regulated by a peptide effector, in addition to experimental example cited by the Examiner. Further elaborating on the passage cited above (page 13, lines 7-25), Example 3 (see page 45) provides a detailed description of the *in vitro* selection and identification of two other examples of polypeptide dependent regulatable, catalytically active nucleic acids, the Cyt18 dependent ribozyme ligase, and the hen egg white lysozyme dependent ribozyme ligase. Although the Cyt18 and lysozyme dependent constructs are sometimes referred to as protein-dependent RCANAs, Appellants have defined the terms "protein", "polypeptide", and "peptide" in the specification (page 32, paragraph 101) as "compounds comprising amino acids joined via peptide bonds", and the terms are used throughout the specification interchangeably. Furthermore, Figure 15(c), Figure 17(c), and Figure 23, each provide a schematic diagram of different selection protocols that can be used to identify and isolate peptide dependent RCANAs, and Figure 22 provides a flow chart of a general method for negative and positive selection of peptide dependent RCANAs.

In addition to providing methods for identification and evidence for the isolation of several peptide dependent RCANAs, Example 3 and Example 4 provide functional data for the physical and chemical properties of the peptide dependent RCANAs identified, *e.g.*, ligand specificity (see Figure 20), and protein dependent catalytic activity (see Figure 21). Appellants also disclose the sequences and structures for several of the protein dependent regulatable, catalytically active nucleic acid sequences identified. Figure 19(a) shows the nucleic acid sequences for six Cyt18 dependent ribozyme ligase clones, and four lysozyme dependent

ribozyme ligase clones, and Figure 19(b) shows the predicted secondary structure of a dominant Cyt18-dependent clone.

Contrary to the Examiner's position that disclosure of a sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence is insufficient to satisfy §112, first paragraph, Appellants contend that one skilled in the art would be able to recognize the catalytic domain of the polynucleotide sequence and its related structure in light of their derivation from well known ribozyme motifs, and be able to distinguish the catalytic domain from the sequence and structure of regulatory domain of the polynucleotide sequence. Furthermore, one skilled in the art would be able to understand the correlation between the sequence and structure of these distinct domains, and the function they each serve. Moreover, the correlation between the structure and function is expressly stated in Claim 1, "the catalytic activity of the catalytic domain is regulated by the interaction of the peptide effector with the regulatory domain".

Appellants further note the core of the instant invention is not so much the specific sequences and structures of the peptide-dependent RCANAs themselves, but rather the very existence of and a method for generating and identifying such peptide-dependent RCANAs, regardless of the sequence or secondary structure, and regardless of how many variant species exist within the genus. Finally, Applicant notes that the Examiner has apparently conceded that the instant invention is enabled, and rejects only on the basis of the written description requirement contained.

Thus, the detailed description of several methods for identifying peptide-dependent RCANAs (see Examples 3 and 4, Figure 15(c), Figure 17(c), Figure 22, Figure 23) combined with the actual reduction to practice of three distinct peptide dependent RCANAs (see Examples

3 and 4), including disclosure of clone sequences (see Figures 19(a)) the predicted secondary structure (see Figure 19(b)), and functional data evidencing the physical and chemical properties of peptide dependent RCANAs identified (see Figures 20 and 21), all clearly indicate the Appellant was in possession of the claimed invention at the time of filing the application.

B. The Rejection of Claims 1-2, 5, 9-10, 128, and 137 under 35 USC § 102(b)

1. Statement of the Relevant Law Pertaining to 35 U.S.C. § 102(b)

35 USC §102(b) provides: A person shall be entitled to a patent unless . . .
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States . . . .

In order for a reference to anticipate, it must contain all the essential elements of the claimed invention (*Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81, 90 (Fed. Cir. 1986)).

2. The Rejection of Claims 1-2, 5, 9-10, 12-13, and 137 under 35 USC § 102(b) is improper

Claims 1-2, 5, 9-10, 12-13, 137 remain rejected under 35 U.S.C. 102(b) as being anticipated by George *et al.*, US Patent No. 5,834,186 ("George"). Appellants respectfully submit that this rejection is improper because George does not teach all the essential elements of the claimed invention and is thus distinguishable from the instant invention.

The Examiner specifically refers to column 3, lines 1-5, in which George discloses catalytic RNA polynucleotides comprising a ribozyme sequence that is linked to a ligand binding sequence wherein the activity of the ribozyme is under the control of that ligand only in the sense that the ligand "regulates" physical access to the catalytic site not the catalytic activity, *i.e.*, the

ligand does not affect the kinetic parameters of the domain. The pending claims in the instant application on the other hand expressly recite catalytically active DNA polynucleotides, not RNA, wherein the ligand actually regulates, *i.e.*, alters the catalytic capabilities of the molecule (as discussed in more detail below). The Examiner also refers to column 2, lines 54-56 in which George discloses that DNA molecules with ligand binding behavior have been isolated by Ellington and Szotak, and Bock *et al.* However, the DNA molecules with ligand binding behavior cited by George are not *regulatable, catalytically active* DNA molecules. There is no teaching in George that would enable a person of ordinary skill in the art to make regulatable, catalytically active DNA molecules without undue experimentation, it is merely prophetic. Thus, George not only does not, it cannot anticipate the instant claims.

The catalytic polynucleotides disclosed in George are distinguishable from the regulatable, catalytically active nucleic acids of the instant invention in that the peptide effector of George does not regulate catalytic activity in the manner of the regulatable, catalytically active DNA molecules of the instant invention . The RNA polynucleotides disclosed by George are "activated" (or "inactivated") by the presence (or absence) of a ligand by causing a change in the conformational shape of the ribozyme upon ligand binding, thereby removing stearic hindrance of the ribozyme's target RNA binding site due to inherent conformational folding. Figure 1(c) in George depicts an inactive ribozyme in which the arms of the ribozyme portion are prevented from binding and cleaving its target RNA due to its conformational folding (see also column 6, lines 1-9). The binding of a specific ligand causes a conformational change in the ribozyme folding, making the target RNA binding site available. Figure 1(d) depicts a ribozyme that is able to bind and cleave target RNA in the absence of a specific ligand, and upon ligand

binding, folds into an inactive conformational shape whereby the target RNA binding site is no longer available (see also Column 6, lines 10-14).

In contrast, the DNA polynucleotides of the claimed instant invention encompass chimeric effector:ribozyme active sites, whereby the effector molecule (*e.g.*, a protein) and the RCANA each contribute a portion of the active site of the ribozyme. The effector does not necessarily cause change in the conformational shape of the catalytic domain, rather it contributes essential residues necessary to turn on catalytic activity. Moreover, the catalytic domain may be inactive or may have low basal activity which is turned on or enhanced upon binding of the peptide effector. This is accomplished by randomizing a portion of the catalytic core itself, whereas George does not teach randomization of any portion of the catalytic core when selecting for peptide dependent regulatable ribozymes or the enhancement of the catalytic activity/rate.

There is literal support in the specification to distinguish the peptide dependent RCANAs of the instant invention from the polynucleotides disclosed in George. Page 14, line 16 to page 15, line 2 states:

> A pool was synthesized in which the random sequence region spanned the catalytic core. Protein-dependent ribozymes were selected from this random sequence pool by selecting for the ability to ligate an oligonucleotide tag in the presence of a protein effector followed by capturing the oligonucleotide tag on an affinity matrix, followed by amplification *in vitro* or *in vivo*. Because the catalytic core has been randomized, the selection for protein dependence not only yields species that may bind to ancillary regions of the ribozyme, but species in which the protein effector actually helps to organize the catalytic core of the ribozyme.
>
> Selection for protein-dependence from a pool in which at least a portion of the catalytic core of the ribozyme is randomized differs from selection for protein-dependence from a pool in which the catalytic core is not randomized. For example, the catalytic core of the protein-dependent ribozymes that was selected differed substantially from the catalytic core

of the original ribozyme and the catalytic core of other, non-protein dependent ribozymes selected based on the original ribozyme.

The specification in fact describes the differences between regulatable, catalytically active nucleic acids of the instant invention from nucleic acids such as those disclosed by George at page 15, lines 20-26:

> Using the methods disclosed herein, it is possible to identify a chimeric effector:ribozyme active site that would lead to catalysis. The invention describes ribozymes that have a detectable, basal chemical reactivity, and that the presence of the effector modulates this basal chemical reactivity. It is for this reason that the present invention differs significantlyfrom other inventions which have claimed protein:RNA complexes in which no basal catalytic activity exists in the ribozyme or protein alone.

The specification also provides an experimental example of the selection, and identification of an RCANA by randomizing the catalytic core. In Example 3 (page 45), the catalytic domain of the ribozyme ligase, LI, was randomized, and variants that required one of two protein cofactors, Cyt18 or hen egg white lysozyme, were selected. Figures 15(a) and 15(b), 17(a) and 17(b) depicts the LI ligase that was the starting point for pool design in these peptide dependent RCANA selections. In the figures the shaded region indicates the catalytic core and ligation junction, and it is apparent that the LI pool contains 50 random sequence positions which overlaps with a portion of the ribozyme (catalytic) core. At Page 47, lines 21-25, Appellant's explain the rationale for randomizing the residues in the catalytic core:

> It was further discovered that larger effector molecules, such as proteins, bind to much larger sites and might sterically inhibit the catalytic core. Therefore, it was necessary to include the catalytic core in the selection. To this end, a nucleic acid segment pool based on the LI Ligase in which critical catalytic residues were also randomized (Figures 15(b) and 17(b)) was designed.

In summary, the §102(b) rejection of claims 1-2, 5, 9-10, 12-13, 137 as being anticipated by George is improper because George is distinguishable from the instant invention. Specifically, the ligand binding of George does not perform the same function as do the effectors (*e.g.*, proteins, peptides) of the present invention which regulate RCANAs of the instant invention. George does not teach randomization of the catalytic core, whereas Appellant's do, and because of such randomization, the effectors in the claimed invention add essential catalytic residues for a given reaction. George does not teach regulatable ribozymes in which basal catalytic activity exists in the ribozyme or protein alone, where as the instant invention encompasses such proteins and ribozymes, whereby catalytic activity is increased or enhanced upon interaction or such protein with such ribozyme. Due to these differences, George cannot anticipate the claimed invention.

VIII. CONCLUSION

For the foregoing reasons, Appellants submit that the pending claims 1-6, 9-14, 128 and 137 are adequately described in the specification under 35 U.S.C. §112, first paragraph, and that the 35 U.S.C. §102(b) rejection is improper. Appellants respectfully request this appeal should be allowed and the Examiner's rejections under 35 U.S.C. § 112, first paragraph and 35 U.S.C. §102(b), should be reversed.

Respectfully submitted,

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IX. CLAIMS APPENDIX

1. (Previously Presented) A DNA polynucleotide that is regulated by a peptide effector comprising:

a regulatable, catalytically active polynucleotide having a catalytic domain and a regulatory domain, wherein the catalytic activity of the catalytic domain is regulated by the interaction of the peptide effector with the regulatory domain.

2. (Previously Presented) The polynucleotide of claim 1, wherein the peptide effector is further defined as being a protein.

3. (Previously Presented) The polynucleotide of claim 1, wherein the peptide effector comprises a peptide of about 7 and 20 amino acids.

4. (Previously Presented) The polynucleotide of claim 1, wherein the peptide effector comprises a peptide of about 7 and 12 amino acids.

5. (Previously Presented) The polynucleotide of claim 1, wherein the catalytic activity of the catalytic domain is specific for a nucleic acid target sequence.

6. (Previously Presented) The polynucleotide of claim 1, wherein the catalytic activity of the catalytic domain is ligation.

7. (Cancelled)

8. (Cancelled)

9. (Original) The polynucleotide of claim 1, wherein the polynucleotide is at least partially single stranded.

10. (Original) The polynucleotide of claim 1, wherein the polynucleotide is at least partially double stranded.

11. (Original) The polynucleotide of claim 1, wherein the polynucleotide comprises at least one modified base.

12. (Previously Presented) The polynucleotide of claim 1, wherein the peptide effector is endogenous.

13. (Previously Presented) The polynucleotide of claim 1, wherein the peptide effector is exogenous.

14. (Previously Presented) The polynucleotide of claim 1, wherein the peptide effector comprises a phosphorylated peptide.

15.-127. (Cancelled)

128. (Previously Presented) A vector comprising:

a regulatable, catalytically active, DNA polynucleotide having a catalytic domain and a regulatory domain, wherein the catalytic activity of the catalytic domain is regulated by the interaction of a peptide effector with the regulatory domain.

129.-136. (Cancelled)

137. (Previously Presented) The polynucleotide of claim 1, wherein the catalytic activity of the catalytic domain is cleavage.